PREVALENCE OF EXTRA-ARTICULAR MANIFESTATIONS IN PATIENTS OF ANKYLOSING SPONDYLITIS

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ABSTRACT

INTRODUCTION

Ankylosing spondylitis is one of the prototypical examples within the group of seronegative spondyloarthropathies. It is associated with extra-articular manifestations, especially uveitis, and less commonly, cardiac and pulmonary disease. In view of this, the present study was undertaken to assess the prevalence of extra-articular manifestations in patients with ankylosing spondylitis.

MATERIALS & METHODS

A hospital based observational study was done among patients who were admitted or attending various Outpatient Departments of Assam Medical College and Hospital, Dibrugarh, Rheumatology Clinic in Assam Medical College & Hospital has been enrolled. 65 patients with ankylosing spondylitis, diagnosed on the basis of Modified New York Criteria were taken in the study. Patients age less than 13 and pregnant women were excluded.

RESULTS

This study showed that amongst the extra-articular manifestations, constitutional symptoms were seen in 46(70.77%) patients, acute anterior uveitis was seen in 13(20%) patients, cardiologic manifestations in 4(6.15%) patients, and pulmonary manifestations were seen in 6(9.23%) patients.

CONCLUSION

The study shows that acute anterior uveitis and cardiopulmonary manifestations were found in significant number of patients with ankylosing spondylitis and cardiopulmonary manifestations were found in patients with a longer duration of disease, and that majority of them were asymptomatic.

KEYWORDS

Ankylosing spondylitis(AS), seronegative spondyloarthropathies, Aortic Regurgitation(AR), LV Diastolic Dysfunction, Restrictive lung disease, Interstitial lung disease.

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INTRODUCTION: Ankylosing spondylitis is a chronic inflammatory disease affecting the axial skeleton, the entheses, and, occasionally, the peripheral joints. The hallmark of Ankylosing spondylitis is inflammatory back pain associated with radiographic sacroiliitis and often spondylitis. In addition to the axial, entheseal, and appendicular skeletal involvement, Ankylosing Spondylitis can also be associated with extra-articular manifestations, especially uveitis, and, less commonly, cardiac and pulmonary disease. The incidence and prevalence of Ankylosing spondylitis generally mirrors the frequency of HLA-B27 in the population (prevalence in India – 6% in normal population and 94% in patients with ankylosing spondylitis).[1]

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HLA-B27 is an important genetic risk factor for these cardiac conditions. Likelihood of cardiac involvement increases with longer duration of disease.[2] The incidence of lung involvement in ankylosing spondylitis, seems to be more pronounced, than thought earlier, with the development of newer imaging technique like HRCT. Although improved techniques in visualization of the lung have allowed identification of more abnormalities of the lung parenchyma associated with AS, there is little known about the natural history of such abnormalities and the potential for therapies used in the treatment of ankylosing spondylitis to halt the progression of the cardio-pulmonary disease. With this background, this study was undertaken to see the clinical profile of ankylosing spondylitis, and its extra-articular manifestations especially cardiac and pulmonary.

MATERIALS & METHODS: A hospital based observational study was carried out on 65 patients of ankylosing spondylitis, who were admitted or attended various Outpatient Departments of Assam Medical College and

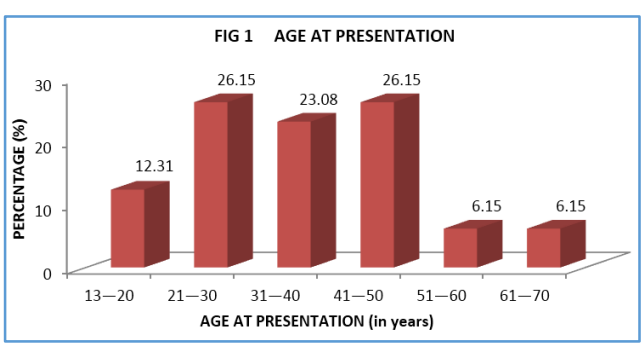
Hospital, Dibrugarh during a period of one year from July 2012 to June 2013.

65 cases of ankylosing spondylitis diagnosed on the basis of Modified New York (1984) criteria were included in the study. All diagnosed cases of ankylosing spondylitis, aged more than equal to 13 years of age, admitted or attending, various Outpatient Departments of Assam Medical College and Hospital, were included in the study after considering the selection criteria and after obtaining the formal informed consent from the patients or relatives. Children less than 13 years of age and pregnant women were excluded from the study. Statistical analysis was performed by using Graph Pad In Stat version 3.10. Continuous data was expressed as mean±standard deviation (SD) and categorical variables as counts and percentages. Linear Regression analysis was used to see correlation. Unpaired t-test and Fisher Exact test was used to calculate P value. P value of <0.05 was considered statistically significant in this study.

RESULTS & OBSERVATIONS: The present study was conducted in the Department of Medicine, Assam Medical College and Hospital. Patients fulfilling the Modified New York Criteria (1984) were included in the study. A total of 65 patients with ankylosing spondylitis were studied. All the cases were subjected to a thorough history, clinical examination and laboratory investigations. The following tables and charts illustrate the results and important features of the study.

Age groups (in years)	Number of patients (n)	Percentage (%)
13—20	8	12.31
21—30	17	26.15
31—40	15	23.08
41—50	17	26.15
51—60	4	6.15
61—70	4	6.15
Total	**65**	**100.00**

Table 1: Age at presentation



The study shows that maximum patients have presented in age group of 21-30 and 41-50 (26.15%). The mean age of presentation was 36.35 years.

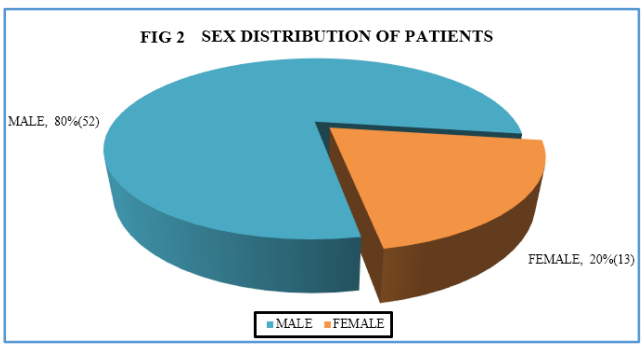
Duration of Disease (in years)	Number of patients (n)	Percentage (%)
≤10	53	81.54
11—20	09	13.85
21—30	02	3.07
31—40	01	1.53
Total	**65**	**100.00**

Table 2: Duration of disease

The above table shows that the duration of disease in 81.54% patients is ≤10 years.

Sex	Number (n)	Percentage (%)	Ratio (Male: Female)
Male	52	80.00	4: 1
Female	13	20.00	
Total	**65**	**100.00**	

Table 3: Sex distribution of patients



The study shows that male to female ratio was 4: 1 (male predominance with 52 cases and 13 females).

Extra-articular Symptoms	Number (n)	Percentage (%)
Acute Anterior Uveitis	13	20.00
GI Manifestations	0	0.00
Cardiac Manifestations	4	6.15
Pulmonary Manifestations	6	9.23
Neurological Manifestations	0	0.00
Renal Manifestations	0	0.00
Constitutional Features	46	70.77

Table 4: Extra-articular manifestations

The above table shows that constitutional symptoms were seen maximum in 70.77% patients and out of the constitutional symptoms fatigue was seen in 66.15% of patients. Acute anterior uveitis was seen in 20%, cardiac manifestations in 6.5% and pulmonary manifestations in 9.23% cases.

Symptoms	Number (n=65)	Percentage (%)
Palpitation	4	6.15
Chest Pain	0	0.00
Dyspnoea on Exertion	6	9.23
Syncope	0	0.00
Cough	0	0.00
Difficulty in Breathing	1	1.54
Haemoptysis	0	0.00

Table 5: Cardio-pulmonary symptoms in AS

The table shows that 9.23% of patients have dyspnoea on exertion and 6.15% of patients have palpitation.

ECG and echocardiographic changes	Number (n=65)	Percentage (%)
First Degree Heart Blocks	2	3.08
Second Degree Heart blocks	0	0.00
Third Degree Heart blocks	0	0.00
ST Changes	0	0.00
Aortic Regurgitation	1	1.54
LV Diastolic Dysfunction	1	1.54

Table 6: ECG and echocardiographic changes in AS

The above table shows that 3.08% of patients have first degree heart block in ECG (these patients were not on any medication), 1.54% of patients were found to have AR (mild valvular AR) and 1.54% patients were found to have LV Diastolic Dysfunction in echocardiography.

Sex	Number (n)	As with cardiac involvement		P value (fisher exact test)
		Number (n)	Percent-age (%)	
Male	52	4	7.69	0.57575
Female	13	0	0.00	
Total	**65**	**4**	**7.69**	

Table 7: Cardiovascular involvement in AS – sex distribution

The above table shows that 7.69% of patients with cardiovascular involvement are all males.

HRCT thorax changes	Number (n=65)	Percentage (%)
Fibrosis of Upper Lobes	2	3.08
Interstitial Lung Disease	1	1.54
Restrictive Lung Disease	2	3.08
Pleural Thickening	1	1.54
Spontaneous Pneumothorax	0	0.00

Table 8: HRCT thorax & PFT changes in AS

The above table shows that on HRCT thorax 3.08% of patients have fibrosis of upper lobes and restrictive lung disease, 1.54% of patients have restrictive lung disease and pleural thickening.

Sex	Number (n)	As with pulmonary involvement		P value (Fisher exact test)
		Number (n)	Percent-age (%)	
Male	52	4	7.69	0.1758
Female	13	2	15.38	
Total	**65**	**6**	**9.23**	

Table 9: Pulmonary involvement in AS: sex distribution

The above table shows that 7.69% of males and 15.38% females have pulmonary manifestations.

Status of cardiac involvement	Duration of disease (mean±sd) in years
As with cardiac involvement	27.5±6.45
As without cardiac involvement	5.3±4.42
P value	< 0.0066

Table 10: Comparison of disease duration in patients with and without cardiac involvement

The above table shows that cardiac manifestation is found in patients with increased duration of disease and it is statistically significant ($p < 0.0066$).

Status of pulmonary involvement	Duration of disease (mean±sd) in years
As with pulmonary involvement	11±2.6
As without pulmonary involvement	6.4±7.1
p value	< 0.0269

Table 11: Comparison of disease duration in patients with and without pulmonary involvement

The above table shows that pulmonary involvement is found in patients with increased duration of disease and it is statistically significant ($p < 0.0269$).

DISCUSSION: The present study was done to evaluate the spectrum of clinical findings in ankylosing spondylitis, especially the extra-articular manifestations.

In the present study, the mean age of presentation was 36.35 years which is similar to the study by Younes et al[3] with mean age of onset 38.9 ± 10.8 years (range, 19–60 years).

In the study, male to female ratio was 4:1 similar to the study by Agarwal et al[4] in which the ratio was 5:1. Male predominance was also seen in a study by Lee et al[5] with male: female ratio of 3:1 and Younes et al[3] with the ratio of 5.25:1.

In the present study constitutional symptoms were present in 70.77% of cases, of which fatigue is most common and acute anterior uveitis was seen in 20.00% cases, all were unilateral. It is similar to 22% of cases seen by Malaviya et al,[1] Agarwal et al[4] with 25.7% cases and Montilla et al[6] found it in 23.5% cases.

In the study, cardiac manifestations were present in 4 patients out of 65(6.15%). All the patients with cardiac manifestations were male (100%) and most of them were asymptomatic at the time of presentation, only one patient with cardiac manifestations had mild dyspnoea on exertion. On evaluation, 2 out of 4 patients had first degree heart block on ECG, one patient had aortic regurgitation and another one had left ventricular diastolic dysfunction on echocardiography. All of these patients were found to be positive for HLAB27. Also when average duration of disease was compared in patients with cardiac involvement and in patients without cardiac involvement, it was found to be 27.5±6.5 years in former group and 5.3±4.42 years in later, which was statistically very significant, with p value of <0.0066. Minimum and maximum values in patients with and without cardiac involvement are 20 and 35 years, 0.5 and 20 years, respectively. Thus the study shows that the prevalence of cardiac involvement is high when duration of disease was more than 20 years.

Malaviya et al[1] found cardiac involvement in 4% of cases, in this study of 51 cases they found aortic incompetence in 2 patients (4%). The duration of disease in these cases was 5 and 14 years, Johnsen et al[7] found AR in 8.8%. All the cases were clinically silent. Yildirir et al[8] found AR in 4.6 % cases, and cardiac involvement was associated with longer duration of disease. Ben et al[9] found cardiovascular manifestations in 10% cases, most common manifestations were AV block in 4.75% cases and AR in 2.4% cases. It was also seen that cardiovascular manifestations in ankylosing spondylitis were associated with longer disease duration. Isohisa et al[10] studied 95 cases for cardiovascular manifestations, male to female ratio in their study was 4.5:1, they found that 99% of cases with cardiovascular manifestations are males.

Thus, frequency of cardiac involvement and its pattern, in respect to male preponderance and disease duration was similar to other studies.

The present study shows that pulmonary manifestations were present in 6 patients out of 65(9.23%). Out of 6 patients, 4 were male (7.69%) and 2 patients were female (15.38%). Most of them were asymptomatic at the time of presentation; only one patient with pulmonary manifestation had difficulty in breathing. Chest x-ray was normal in all the patients. On evaluation with HRCT thorax, 2 patients were found to have upper lobe fibrosis, 1 patient had ILD and another one had pleural thickening and 2 patients show restrictive pattern in PFT. In our study, we found out that pulmonary involvement in patients with AS was high when average duration of disease was 11±2.6 years.

Malaviya et al[1] in the study found pulmonary involvement in 4% of cases, out of 51 cases 2 patients had apical pulmonary fibrosis. Rosenow et al[11] in their study of 2080 patients, pleuropulmonary manifestations were seen in 1.3% cases, and most common finding was apical lobe fibrosis. In the study of 55 cases of AS by Maghraoui et al[12] it was seen that most common lung abnormality was apical lobe fibrosis and bronchiectasis. Thus, the pattern of lung involvement in the present study was similar to other Indian and International studies.

CONCLUSION: This study was done with special interest on extra-articular manifestations and it was seen that acute anterior uveitis and cardiopulmonary involvement was present in significant number of patients, and cardiopulmonary involvement was seen in patients with longer duration of disease, and majority of them were asymptomatic. Thus, the cardiopulmonary manifestations if diagnosed early when it is still in subclinical state can be treated accordingly to prevent further complications.

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